IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Reissue Application For:	United States Patent No. 5,688,657
Title:	MONOCLONAL ANTIBODIES AGAINST CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR
Patent Appln. Filed:	September 12, 1994
Patent Issued:	November 18, 1997
Assignee:	International Bio-Immune Systems, Inc.
Patent Group Art Unit:	1652
Reissue Applicants:	Kwong Y. Tsang and Myron Arlen
Reissue Serial No.	09/633,034 Atty Docket No. 33081-R 072771.0106
Reissue Appln Filed:	August 4, 2000

REISSUE DECLARATION

I hereby certify that this paper is being deposited on 11/05/04 with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450

Lisa B. Kole
Attorney Name

Lisa B. Kole
Signature

35,225
PTO Registration No.

11/05/04
Date of Signature

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

WE, Kwong Y. Tsang and Myron Arlen, the below named inventors, hereby declare as follows:

Our residences, post office addresses and citizenships are as stated below our signatures, *infra*.

We believe that we are the original, first and joint inventors of the invention described and claimed in United States Letters Patent No. 5.688.657 ("the '657 patent"), entitled "MONOCLONAL ANTIBODIES AGAINST CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR," which issued on November 18, 1997, and of the above-identified reissue application, which is appended hereto and by which we solicit a reissue patent.

I. REVIEW OF PAPERS AND DUTY OF CANDOR

We have reviewed and understand the contents of the above-identified patent, including the issued claims, and the above-identified reissue application, including the claims thereof.

We acknowledge the duty to disclose information which is material to the examination of this reissue application, in accordance with 37 C.F.R. §1.56.

II. PRIORITY CLAIM

The above-identified reissue application is based on the '657 patent which is a continuation-in-part of Serial No. 08/159,836, filed November 30, 1993, now abandoned, which is a continuation-in part of Serial No. 08/117,430, filed September 7, 1993, now abandoned, which is a continuation-in-part of Serial No. 07/670,816, now abandoned, which is a continuation-in-part of Serial No. 07/176,337, filed March 31, 1988, now abandoned.

III. OFFER TO SURRENDER ORIGINAL LETTERS PATENTS

We and our assignee hereby offer to surrender the original letters patent, or provide an appropriate affidavit or declaration in the event that the original patent is lost, upon an indication of allowability of this reissue patent application.

IV. STATEMENT OF INOPERATIVENESS OF THE ISSUED PATENT

We believe the original patent to be wholly or partly inoperative because of several errors that arose without any deceptive intention on our parts as applicants therefor.

First, inadvertent errors during the prosecution of the application that issued as the '657 patent resulted in erroneous deposits of the hybridoma cell lines referred to in the patent as PCA 31.1 and PCA 33.28, corresponding to ATCC Accession Nos. HB-12314 and HB-12315,

respectively. Second, the specification and claims indicate that the colon carcinoma associated antigens identified do not occur on any carcinomas other than colon carcinoma, when the specification provides data that indicates that these antigens are indeed present on certain other forms of human carcinoma (but not normal tissue). Third, claims 22, 23 and 47 erroneously state that the target antigen in a test sample is "purified," which makes these claims wholly or partly inoperative.

Each of these inadvertent errors are discussed in greater detail below.

V. SPECIFICATION OF "ERRORS" RELIED UPON AND HOW THEY AROSE

The following is a description of the manner in which the errors specified below are believed to have occurred. Although the following account does not describe our own actions, on information and belief we believe it to be true.

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Concerned about the identity of the murine hybridoma cell line, IBS obtained the DNA sequence encoding a portion of the variable heavy chain region of the monoclonal antibody secreted by the cell line and determined that the cell line was not producing the expected 31.1 antibody. With regard to the 33.28 antibody, when immunohistochemical studies were performed, the secreted antibody was found not to have the expected immunospecificity.

It is now believed that an employee of IBS had, without deceptive intent, mistakenly mislabeled tubes believed to contain both the murine hybridoma cell lines producing the 31.1 and 33.28 monoclonal antibodies when preparing frozen samples of the cells for storage purposes. The samples of hybridoma cells deposited with the ATCC are believed to have been prepared from cultures derived from mislabeled frozen cells, thus resulting in erroneous deposits of the HB-12314 and HB-12315 hybridoma cell lines referred to in the '675 patent. Accordingly, the mAbs made available via the ATCC depository are believed not to be the monoclonal antibodies claimed, and hence the specification of the '657 patent is defective.

In addition, the specification and claims of the '657 patent erroneously state, at various sections of text, that the colon carcinoma associated antigens generally claimed are not found on human carcinoma cells other than colon carcinoma cells (see, for example, the specification at column 3, lines 58-62 and claims 1, 30 , 34 and 38). These statements are contradicted by statements and data presented in the '657 patent specification, including (1) the patent specification at column 4, lines 33-35, which states "the antigens are tumor specific, being present in the malignancies of colon, *breast and ovarian cancer*" (emphasis added); (2) Example XI at column 29, line 61 through column 30, line 12, which states that "[t]hese results indicate that the antigens defined by mAbs 31.1 and 33.28 are expressed in a select group of women with breast disease and would be useful for diagnosis of said disease;" and (3) Example XII at column 30, lines 15-20, which states that "[t]hese results indicate that the antigens defined by mAbs 31.1 and 33.28 are expressed in a select group of women with ovarian cancer and would be useful for diagnosis of said disease." Thus, the recitations in the specification which indicate that the colon carcinoma associated antigens are not expressed in any other cancers are erroneous.

Other text erroneously indicates that the antigens have been found to be expressed *only* in colon, breast and ovarian cancer (see, *e.g.*, column 3, lines 51-57), statements which are contradicted by Table 1 at column 23, which shows that mAb 31.1 bound to two out of three pancreatic cell lines tested, and Table 8 at column 28, which shows that mAb 31.1 bound to a stomach cancer cell sample.

Each of the erroneous statements regarding tumor specificity were made without deceptive intent. We would add that we continue to believe that the defined antigens are not associated with all types of tumors, so that the statement "the antigens are tumor-specific, being

present in the malignancies of colon, breast and ovarian cancer" (as found recited several times in the '657 patent specification, including at column 3 lines 33-35) remains true even if certain other types of cancer cells express the antigen. Similarly, the statement : "the immunogenicity in humans is specific, in that only colon, breast and ovarian cancer patients, but not patients with other forms of cancer, show evidence of specific in vivo or in vitro immunological reactivity to the antigens" (as found recited several times in the '657 patent specification, including at column 3 lines 39-43) was true at the time the specification was originally filed. However, data in the '657 patent itself, and subsequent research, supports the conclusion that the antigen defined by at least monoclonal antibody 31.1 is not associated *only* with those cancers.

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We have reviewed and understand the amendments to the specification and claims of the '657 patent set forth in the RESPONSE submitted herewith, which, among other things, (1) now recite the new ATCC accession numbers of the hybridoma cells deposited during the pendency of this reissue application; (2)focus the claims on monoclonal antibodies 31.1 and 33.28 and chimeric antibody Chi #1, antibodies that competitively inhibit the binding of these specific antibodies to their target antigens, and antibodies directed against the target antigens defined by these specific antibodies; (3) correct the erroneous statements relating to antigen specificity and purity of antigen in a sample; and (4) correct various typographical errors.

Every error in the patent which is corrected in the present reissue application, and is not covered by a prior oath/declaration submitted in this application, arose without any deceptive intention on the part of the applicants.

VI. POWER OF ATTORNEY

Applicants and the assignee hereby appoint the following attorneys of the firm of Baker Botts L.L.P., having an address at 30 Rockefeller Plaza, New York, New York 10112 as their attorneys, with full power of substitution and revocation, to prosecute this reissue application and to transact all business in the Patent and Trademark Office connected therewith: Robert C. Sheinfeld, Reg. No. 31,300, Rochelle K. Seide, Reg. No. 32,300, Gary Butter, Reg. No., 33,841, and Lisa B. Kole, Reg. No. 35,225.

Please address all communications regarding this application to:

Lisa B. Kole, Esq.
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30 Rockefeller Plaza
New York, New York 10112

VII. DECLARATION

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Inventor	:	Kwong Y. Tsang
Inventor's Signature	:	_____
Date of Signature	:	_____
Residence	:	_____
Citizenship	:	_____
Post Office Address	:	_____
		_____

Inventor	:	Myron Arlen
Inventor's Signature	:	Myron Arlen
Date of Signature	:	11/1/04
Residence	:	81 Wensley Dr.
Citizenship	:	Great Neck NY 11020
Post Office Address	:	_____
		_____

ASSENT BY ASSIGNEE

International Bio-Immune Systems, Inc. the assignee of the entire right, title and interest in United States Patent No. 5,688,657, entitled "MONOCLONAL ANTIBODIES AGAINST CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR," pursuant to the assignment recorded in the records of the United States Patent Office at reel 6895, frame 803, hereby assents to the filing of the reissue application for said Patent No. 5,688,657 that is attached to this Declaration, and confirms reissue applicant's offer to surrender the original '657 patent as stated therein, and to the appointment of power of attorney as stated therein.

International Bio-Immune Systems, Inc.

By: _____

Leslie Stern

Chief Executive Officer

Date: _____

33081-R 072771.0106

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Inventor	:	Kwong Y. Tsang
Inventor's Signature	:	_____
Date of Signature	:	_____
Residence	:	_____
Citizenship	:	_____
Post Office Address	:	_____
		_____

Inventor	:	Myron Arlen
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By: _____

Leslie Stern

Chief Executive Officer

Date: NOVEMBER 4, 2004

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Lisa B. Kole
Attorney Name

Signature

35,225
PTO Registration No.

11/05/04
Date of Signature

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

International Bio-Immune Systems, Inc.(hereafter, "IBS"), as the assignee of the entire right, title and interest in United States Patent No. 5,688,657, on which the above-identified reissue application is based, declares as follows.

IBS is a corporation having an address at 225 West Community Drive, Suite 140, Great Neck, New York 11021. IBS believes that the above-identified reissue application does not seek to enlarge the claims of the original patent.

I. REVIEW OF PAPERS AND DUTY OF CANDOR

IBS has reviewed and understands the contents of the above-identified patent, including the issued claims, and the above-identified reissue application, including the claims thereof.

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Other text erroneously indicates that the antigens have been found to be expressed *only* in colon, breast and ovarian cancer (see, *e.g.*, column 3, lines 51-57), statements which are contradicted by Table 1 at column 23, which shows that mAb 31.1 bound to two out of three pancreatic cell lines tested, and Table 8 at column 28, which shows that mAb 31.1 bound to a stomach cancer cell sample.

Each of the erroneous statements regarding tumor specificity were made without deceptive intent. IBS believes that the defined antigens are not associated with all types of tumors, so that the statement "the antigens are tumor-specific, being present in the malignancies of colon, breast and ovarian cancer" (as found recited several times in the '657 patent specification, including at column 3 lines 33-35) remains true even if certain other types of cancer cells express the antigen. Similarly, the statement : "the immunogenicity in humans is specific, in that only colon, breast and ovarian cancer patients, but not patients with other forms

of cancer, show evidence of specific in vivo or in vitro immunological reactivity to the antigens" (as found recited several times in the '657 patent specification, including at column 3 lines 39-43) was true at the time the specification was originally filed. However, data in the '657 patent itself, and subsequent research, supports the conclusion that the antigen defined by at least monoclonal antibody 31.1 is not associated *only* with those cancers.

Further, it has been noted that claims 22, 23 and 47 contain an error, in that they relate to immunoassays for detecting the presence of colon carcinoma associated antigen in a sample. Both of these claims now recite steps for exposing the sample to antibody and then "detecting the binding of the antibody to the purified colon carcinoma associated protein antigen," which is an obvious error, since the antigen in the sample is not purified. This error in reciting "purified" was made without deceptive intent.

IBS is aware that during the prosecution of this reissue application, new deposits of true samples of the hybridomas PCA 31.1 and PCA 33.28, producing monoclonal antibodies 31.1 and 33.28, respectively, as referred to in the '657 patent, have been deposited with the ATCC under the terms of the Budapest Treaty, to correct the errors made in materials initially deposited with the ATCC.

IBS has reviewed and understands the amendments to the specification and claims of the '657 patent set forth in the RESPONSE submitted herewith, which, among other things, (1) now recite the new ATCC accession numbers of the hybridoma cells deposited during the pendency of this reissue application; (2)focus the claims on monoclonal antibodies 31.1 and 33.28 and chimeric antibody Chi #1, antibodies that competitively inhibit the binding of these specific antibodies to their target antigens, and antibodies directed against the target antigens defined by these specific antibodies; (3) correct the erroneous statements relating to antigen specificity and purity of antigen in a sample; and (4) correct various typographical errors.

Every error in the patent which is corrected in the present reissue application, and is not covered by a prior oath/declaration submitted in this application, arose without any deceptive intention.

VI. POWER OF ATTORNEY

IBS hereby appoints the following attorneys of the firm of Baker Botts L.L.P., having an address at 30 Rockefeller Plaza, New York, New York 10112 as their attorneys, with full power of substitution and revocation, to prosecute this reissue application and to transact all business in the Patent and Trademark Office connected therewith: Robert C. Sheinfeld, Reg. No. 31,300, Rochelle K. Seide, Reg. No. 32,300, Gary Butter, Reg. No., 33,841, and Lisa B. Kole, Reg. No. 35,225.

Please address all communications regarding this application to:

Lisa B. Kole, Esq.
Baker Botts L.L.P.
30 Rockefeller Plaza
New York, New York 10112

VII. DECLARATION

IBS hereby declares that all statements made herein of its own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

International Bio-Immune Systems, Inc.
By: Leslie F. Stern
Leslie Stern
Chief Executive Officer
Date: 11/5/04

ASSENT BY ASSIGNEE

International Bio-Immune Systems, Inc. the assignee of the entire right, title and interest in United States Patent No. 5,688,657, entitled "MONOCLONAL ANTIBODIES AGAINST CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR," pursuant to the assignment recorded in the records of the United States Patent Office at reel 6895, frame 803, hereby assents to the filing of the reissue application for said Patent No. 5,688,657 that is attached to this Declaration, and confirms reissue applicant's offer to surrender the original '657 patent as stated therein, and to the appointment of power of attorney as stated therein.

International Bio-Immune Systems, Inc.

By: _____

Leslie Stern

Chief Executive Officer

Date: 11/5/04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tsang et al.

Serial No.: 09/633,034, an application for reissue of United States Patent No. 5,688,657 Examiner: Helms, L.R..

Filed : August 4, 2000 Group Art Unit: 1642

Atty Docket: 33081-R 072771.0106

For : MONOCLONAL ANTIBODIES AGAINST HUMAN COLON CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR

DECLARATION OF DR. MYRON ARLEN

I hereby certify that this paper is being deposited on 11/5/04 with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450

Lisa B. Kole
Attorney Name

Lisa B Kole
Signature

35,225
PTO Registration No.

11/5/04
Date of Signature

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

I, Dr. Myron Arlen, declare the following:

1. I am a co-inventor of the invention contained in the above-identified United States Patent and this reissue application.

2. During the prosecution of the application which issued as United States Patent No. 5,688,657, cell lines believed to be hybridoma cell lines PCA 31.1 and PCA 33.28 were deposited with the American Type Culture Collection ("ATCC"). It was subsequently

discovered that the deposited cell lines were not, in fact, hybridoma cell lines PCA 31.1 and 33.28. We believe this error to have been made inadvertently, without deceptive intent. The discovery of the error prompted the filing of this reissue application.

3. To correct the erroneous deposits, correct samples of both PCA 31.1 and PCA 33.28 cell lines, as referred to in the specification of the '657 patent and this reissue application, producing, respectively, monoclonal antibodies 31.1 and 33.28, as referred to in the '657 patent and this reissue application, were deposited with the ATCC, under the terms of the Budapest Treaty, after the effective filing date of the above-identified reissue application and its parent application. Specifically, PCA 31.1 was deposited on September 22, 2000 and was subsequently assigned Accession No. PTA-2497, and PCA 33.28 was deposited on August 26, 2003 and was subsequently assigned Accession No. PTA-5413. Therefore, upon issuance of this reissue application, the hybridoma cell lines identified in the specification will be available to the public.

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this reissue application or any patent issued thereon.

Myron Arlen MD

Dr. Myron Arlen

11/1/04

Date